CLAIMS

What we claim is:

1. A vaccine comprising a free-living microbe, wherein the nucleic acid of the microbe has been modified by reaction with a nucleic acid targeted compound that reacts directly with the nucleic acid so that the microbe is attenuated for proliferation.

2. The vaccine of claim 1, wherein the nucleic-acid targeted compound is a nucleic acid alkylator.

3. The vaccine of claim 2, wherein the nucleic acid alkylator is β-alanine, N-(acridin-9-yl), 2-[bis(2-chloroethyl)amino]ethyl ester.

4. The vaccine of claim 1, wherein the nucleic acid targeted compound is activated by irradiation.

5. The vaccine of claim 4, wherein the nucleic acid targeted compound is a psoralen compound activated by UVA irradiation.

6. The vaccine of claim 5, wherein the nucleic acid targeted compound is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen.

7. The vaccine of claim 1, wherein the microbe comprises a genetic mutation that attenuates the ability of the microbe to repair its nucleic acid that has been modified.

8. The vaccine of claim 7, wherein the microbe is defective with respect to a DNA repair enzyme.

9. The vaccine of claim 8, wherein the genetic mutation is in one or more gene selected from the group consisting of *phr*B, *uvr*A, *uvr*B, *uvr*C, *uvr*D and *rec*A, or in a

functional equivalent of one or more gene selected from the group consisting of *phr*B, *uvr*A, *uvr*B, *uvr*C, *uvr*D and *rec*A.

10. The vaccine of claim 9, wherein the microbe comprises genetic mutations in both *uvrA* and *uvrB*, or in functional equivalents of both *uvrA* and *uvrB*.

11. The vaccine of claim 8, which is defective with respect to RecA, or the functional equivalent of RecA.

12. The vaccine of claim 1, wherein the microbe is a bacterium.

13. The vaccine of claim12, wherein the microbe is *Mycobacterium tuberculosis*.

14. The vaccine of claim 12, wherein the microbe is *Bacillus anthracis*.

15. The vaccine of claim 12, wherein the microbe is *Listeria monocytogenes*.

16. The vaccine of claim 15, wherein the microbe comprises at least one mutation in both *uvrA* and *uvrB*.

17. The vaccine of claim 16, wherein the microbe further comprises a mutation in the *actA* gene, the *inlB* gene, or both genes.

18. The vaccine of claim 1, wherein the microbe comprises a heterologous nucleic acid sequence encoding an antigen.

19. The vaccine of claim 1, wherein the vaccine further comprises a pharmaceutically acceptable carrier or an adjuvant.

20. A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of the vaccine of claim 1.

21. A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of the vaccine of claim 1, wherein the microbe expresses the antigen.

22. An isolated professional antigen-presenting cell comprising a free-living microbe, wherein the nucleic acid of the microbe has been modified by reaction with a nucleic acid targeted compound that reacts directly with the nucleic acid so that the microbe is attenuated for proliferation.

23. The professional antigen-presenting cell of claim 22, which is a dendritic cell.

24. The professional antigen-presenting cell of claim 22, wherein the nucleic-acid targeted compound is a nucleic acid alkylator.

25. The professional antigen-presenting cell of claim 24, wherein the nucleic acid alkylator is β-alanine, N-(acridin-9-yl), 2-[bis(2-chloroethyl)amino]ethyl ester.

26. The professional antigen-presenting cell of claim 22, wherein the nucleic acid targeted compound is activated by irradiation.

27. The professional antigen-presenting cell of claim 26, wherein the nucleic acid targeted compound is a psoralen compound activated by UVA irradiation.

28. The professional antigen-presenting cell of claim 27, wherein the nucleic acid targeted compound is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen.

29. The professional antigen-presenting cell of claim 22, wherein the microbe comprises a genetic mutation that attenuates the ability of the microbe to repair its nucleic acid that has been modified.

30. The professional antigen-presenting cell of claim 29, wherein the microbe is defective with respect to a DNA repair enzyme.

31. The professional antigen-presenting cell of claim 30, wherein the genetic mutation is in one or more gene selected from the group consisting of *phr*B, *uvr*A, *uvr*B, *uvr*C, *uvr*D and *rec*A, or in a functional equivalent of one or more gene selected from the group consisting of *phr*B, *uvr*A, *uvr*B, *uvr*C, *uvr*D and *rec*A.

32. The professional antigen-presenting cell of claim 31, wherein the microbe comprises genetic mutations in both *uvrA* and *uvrB*, or in functional equivalents of both *uvrA* and *uvrB*.

33. The professional antigen-presenting cell of claim 31, wherein the microbe is defective with respect to RecA, or a functional equivalent of Rec A.

34. The professional antigen-presenting cell of claim 23, wherein the microbe is a bacterium.

35. The professional antigen-presenting cell of claim 34, wherein the microbe is *Mycobacterium tuberculosis*.

36. The professional antigen-presenting cell of claim 34, wherein the microbe is *Listeria monocytogenes*.

37. The professional antigen-presenting cell of claim 32, wherein the microbe comprises at least one mutation in both *uvrA* and *uvrB*.

38. The professional antigen-presenting cell of claim 22, wherein the microbe comprises a heterologous nucleic acid sequence encoding an antigen.

39. A vaccine comprising the professional antigen-presenting cell of claim 22.

40. A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of the professional antigen-presenting cell of claim 22.

41. A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of the professional antigen-presenting cell of claim 22, wherein the microbe comprises a nucleic acid sequence encoding the antigen.

42. A method of activating naïve T cells *ex vivo* or *in vitro*, comprising contacting the naïve T cells with the professional antigen-presenting cell of claim 22 under suitable conditions and for a sufficient time to activate the naïve T cells.

43. A method of loading professional antigen-presenting cells with an antigen comprising contacting the professional antigen-presenting cells with a free-living microbe that comprises a nucleic acid sequence encoding the antigen, under suitable conditions and for a sufficient time to load the professional antigen-presenting cells, wherein the nucleic acid of the microbe has been modified by reaction with a nucleic acid targeted compound that reacts directly with the nucleic acid so that the microbe is attenuated for proliferation.

44. A method of activating and/or maturing professional antigen-presenting cells comprising contacting the professional antigen-presenting cells with a free-living microbe that comprises a nucleic acid sequence encoding an antigen, under suitable conditions and for a sufficient time to activate and/or to allow the maturation of the professional antigen-presenting cells, wherein the nucleic acid of the microbe has been modified by reaction with a nucleic acid targeted compound that reacts directly with the nucleic acid so that the microbe is attenuated for proliferation.

45. A method of preventing or treating a disease in a host, comprising the following steps. (a) loading professional antigen-presenting cells with an antigen by contacting the

cells with a free-living microbe that comprises a nucleic acid sequence encoding an antigen, wherein the nucleic acid of the microbe has been modified by reaction with a nucleic acid targeted compound that reacts directly with the nucleic acid so that the microbe is attenuated for proliferation; and (b) administering an effective amount of a composition comprising the loaded professional antigen-presenting cells to the host.

46. A method of inducing an immune response to an antigen in a host, comprising the following steps. (a) loading professional antigen-presenting cells with the antigen by contacting the cells with a free-living microbe that comprises a nucleic acid sequence encoding the antigen, wherein the nucleic acid of the microbe has been modified by reaction with a nucleic acid targeted compound that reacts directly with the nucleic acid so that the microbe is attenuated for proliferation; and (b) administering an effective amount of a composition comprising the loaded professional antigen-presenting cells to the host.

47. An isolated mutant *Listeria monocytogenes* strain comprising a genetic mutation that attenuates its ability to repair its nucleic acid.

48. The mutant strain of claim 47, which is defective with respect to at least one DNA repair enzyme.

49. The mutant strain of claim 47 which is attenuated with respect to UvrA, UvrB, or both UvrA and UvrB.

50. The mutant strain of claim 49, which comprises a genetic mutation in the *uvrA* gene, the *uvrB* gene, or both the *uvrA* and *uvrB* genes.

51. The mutant strain of claim 47, wherein the nucleic acid of the bacteria of the strain have been modified so that the bacteria are attenuated for proliferation.

52. The mutant strain of claim 47, which is selected from the group consisting of a *Listeria monocytogenes actA⁻/uvrAB⁻* strain deposited with the American Type Culture Collection (ATCC) and identified by accession number PTA-5563, or a mutant of the deposited strain which is defective with respect to UvrA, UvrB, and ActA.

53. The mutant strain of claim 52, which is the *Listeria monocytogenes actA⁻/inlB⁻* strain deposited with the American Type Culture Collection (ATCC) and identified by accession number PTA-5562.

54. A vaccine comprising (a) the mutant strain of claim 47, and (b) a pharmaceutically acceptable carrier or adjuvant.

55. A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of a composition comprising the strain of claim 47, wherein the strain comprises a nucleic acid molecule encoding the antigen.

56. A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of a composition comprising the strain of claim 47.

57. A professional antigen-presenting cell comprising the strain of claim 47.

58. An isolated mutant *Bacillus anthracis* strain comprising a genetic mutation that attenuates its ability to repair its nucleic acid.

59. The mutant strain of claim 58, which is defective with respect to at least one DNA repair enzyme.

60. The mutant strain of claim 59 which is attenuated with respect to UvrA, UvrB, or both UvrA and UvrB.

61. The mutant strain of claim 60, which comprises a genetic mutation in the *uvrA* gene, the *uvrB* gene, or both the *uvrA* and *uvrB* genes.

62. The mutant strain of claim 58, which comprises one or more mutations in the *lef* gene, the *cya* gene, or both genes that decreases the toxicity of the strain.

63. The mutant strain of claim 58, wherein the nucleic acid of the bacteria of the strain have been modified so that the bacteria are attenuated for proliferation.

64. A method of inducing an immune response in a host to a *Bacillus anthracis* antigen comprising administering to the host an effective amount of a composition comprising the mutant strain of claim 58.

65. A method of preventing or treating a *Bacillus anthracis* infection in a host, comprising administering to the host an effective amount of a composition comprising the mutant strain of claim 58.

66. A vaccine comprising a free-living microbe which is defective with respect to at least one DNA repair enzyme.

67. The vaccine of claim 66, wherein the microbe comprises a genetic mutation in one or more gene selected from the group consisting of *phr*B, *uvr*A, *uvr*B, *uvr*C, *uvr*D and *rec*A, or in a functional equivalent of one or more gene selected from the group consisting of *phr*B, *uvr*A, *uvr*B, *uvr*C, *uvr*D and *rec*A.

68. The vaccine of claim 67, wherein the microbe comprises genetic mutations in both *uvrA* and *uvrB*, or in functional equivalents of both *uvrA* and *uvrB*.

69. The vaccine of claim 66, which is defective with respect to RecA, or the functional equivalent of RecA.

70. The vaccine of claim 66, wherein the microbe is a bacterium.

71. The vaccine of claim 66, wherein the microbe comprises a heterologous nucleic acid sequence encoding an antigen.

72. The vaccine of claim 66, wherein the vaccine further comprises a pharmaceutically acceptable carrier or an adjuvant.

73. A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of the vaccine of claim 66.

74. A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of the vaccine of claim 66, wherein the microbe expresses the antigen.

75. An isolated professional antigen-presenting cell comprising a free-living microbe which is defective with respect to at least one DNA repair enzyme.

76. The antigen-presenting cell of claim 75, wherein the microbe comprises a genetic mutation in one or more gene selected from the group consisting of *phr*B, *uvr*A, *uvr*B, *uvr*C, *uvr*D and *rec*A, or in a functional equivalent of one or more gene selected from the group consisting of *phr*B, *uvr*A, *uvr*B, *uvr*C, *uvr*D and *rec*A.

77. The antigen-presenting cell of claim 76, wherein the microbe comprises genetic mutations in both *uvrA* and *uvrB*, or in functional equivalents of both *uvrA* and *uvrB*.

78. The antigen-presenting cell of claim 75, which is defective with respect to RecA, or the functional equivalent of RecA.

79. The antigen-presenting cell of claim 75, wherein the microbe is a bacterium.

80. The antigen-presenting cell of claim 75, wherein the microbe comprises a heterologous nucleic acid sequence encoding an antigen.

81. A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of the antigen-presenting cell of claim 75.

82. A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of the antigen-presenting cell of claim 75, wherein the microbe expresses the antigen.